Intracellular pH measurements using perfluorocarbon nanoemulsions.

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Public Summary:
We report the synthesis and formulation of unique perfluorocarbon (PFC) nanoemulsions enabling intracellular pH measurements in living cells via fluorescent microscopy and flow cytometry. These nanoemulsions are formulated to readily enter cells upon coincubation and contain two cyanine-based fluorescent reporters covalently bound to the PFC molecules, specifically Cy3-PFC and CypHer5-PFC conjugates. The spectral and pH-sensing properties of the nanoemulsions were characterized in vitro and showed the unaltered spectral behavior of dyes after formulation. In rat 9L glioma cells loaded with nanoemulsion, the local pH of nanoemulsions was longitudinally quantified using optical microscopy and flow cytometry and displayed a steady decrease in pH to a level of 5.5 over 3 h, indicating rapid uptake of nanoemulsion to acidic compartments. Overall, these reagents enable real-time optical detection of intracellular pH in living cells in response to pharmacological manipulations. Moreover, recent approaches for in vivo cell tracking using magnetic resonance imaging (MRI) employ intracellular PFC nanoemulsion probes to track cells using (19)F MRI. However, the intracellular fate of these imaging probes is poorly understood. The pH-sensing nanoemulsions allow the study of the fate of the PFC tracer inside the labeled cell, which is important for understanding the PFC cell loading dynamics, nanoemulsion stability and cell viability over time.

Scientific Abstract:
We report the synthesis and formulation of unique perfluorocarbon (PFC) nanoemulsions enabling intracellular pH measurements in living cells via fluorescent microscopy and flow cytometry. These nanoemulsions are formulated to readily enter cells upon coincubation and contain two cyanine-based fluorescent reporters covalently bound to the PFC molecules, specifically Cy3-PFC and CypHer5-PFC conjugates. The spectral and pH-sensing properties of the nanoemulsions were characterized in vitro and showed the unaltered spectral behavior of dyes after formulation. In rat 9L glioma cells loaded with nanoemulsion, the local pH of nanoemulsions was longitudinally quantified using optical microscopy and flow cytometry and displayed a steady decrease in pH to a level of 5.5 over 3 h, indicating rapid uptake of nanoemulsion to acidic compartments. Overall, these reagents enable real-time optical detection of intracellular pH in living cells in response to pharmacological manipulations. Moreover, recent approaches for in vivo cell tracking using magnetic resonance imaging (MRI) employ intracellular PFC nanoemulsion probes to track cells using (19)F MRI. However, the intracellular fate of these imaging probes is poorly understood. The pH-sensing nanoemulsions allow the study of the fate of the PFC tracer inside the labeled cell, which is important for understanding the PFC cell loading dynamics, nanoemulsion stability and cell viability over time.